

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE  <b>ANNUAL REPORT OF RESEARCH FACILITY</b> ( TYPE OR PRINT )	1. CERTIFICATE NUMBER: 33-R-0029 CUSTOMER NUMBER: 603	FORM APPROVED OMB NO. 0579-0036
University Of Illinois At Urbana-Champaign 1 Observatory Building 901 S. Mathews Urbana, IL 61801  Telephone: (217) -333-2564		

**3. REPORTING FACILITY** ( List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary )

FACILITY LOCATIONS ( Sites ) - See Attached Listing

**REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY ( Attach additional sheets if necessary or use APHIS Form 7023A )**

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reason such drugs were not used must be attached to this report )	F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E )
4. Dogs		211	396		607
5. Cats		74	286		360
6. Guinea Pigs		11			11
7. Hamsters		4			4
8. Rabbits		125	24		149
9. Non-human Primates		-	-	-	-
10. Sheep		70			70
11. Pigs		666	190	135	991
12. Other Farm Animals					
Cattle		118	6		124
Llama		4			4
13. Other Animals					
Horse		29	42		71
Goat		3			3
Chinchilla			15	27	42

**ASSURANCE STATEMENTS**

- 1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
- 2) Each principal investigator has considered alternatives to painful procedures.
- 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and an Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
- 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL  
 ( Chief Executive Officer or Legally Responsible Institutional Official )

(B)(6) (B)(7)(c)	DATE SIGNED 11/29/07
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(B)(6) (B)(7)(c)

## APHIS Form 7023 Site List

The following sites have been reported by the facility.

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Registration Number: 33-R-0029  
Customer Number: 603  
Facility: University of Illinois at Urbana-Champaign  
1 Observatory Building  
901 S. Mathews  
Urbana, IL 61801  
217-333-2564 (phone)  
217-244-7963 (fax)

Facilities reported

(b)(2)High, (b)(7)f

## Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: **33-R-0029**
2. Number 27 of animals used in this study.
3. Species (common name) Chinchilla of animals used in the study.
4. Explain the procedure producing pain and/or distress.

Because we are studying middle ear infection, the infected chinchillas, especially at later stage of infection (Day 5-7) may lose balance and be unable to move, and consequently, unable to gain access to water and food. If this should occur, the chinchillas will be euthanized immediately.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see question 6 below).

The animals will be observed four times a day (6 am, noon, 6pm and midnight) from inoculation to euthanizing. Animals meeting the euthanasia criteria (agonal or unable to feed and drink) will be immediately euthanized by carbon dioxide asphyxiation using compressed gas as the CO<sub>2</sub> source, or by intraperitoneal injection of sodium pentobarbital (200 mg/kg body weight)

No analgesics will be administered to the animals used in all these studies. The primary reason for not giving analgesics in our studies is that these drugs alter or inhibit the immune reactions we wish to study and would reduce the value of those studies. For example, it is well known that the morphine analogs and endorphins have a significant effect on immune responses as well as regional blood flow and even outcome following injury. In mice phagocytic function of macrophages and polymorphonuclear cells are clearly reduced by morphine. Lymphocyte proliferation, a typical study endpoint in trauma studies, is reduced by morphine. Morphine acts to suppress the immune system, and results in accelerated death in an experimental model of sepsis. Furthermore, naloxone, an antagonist of the morphine-like alkaloids, improves survival in shock. The morphine derivative, buprenorphine, was shown to reduce the serum levels of TNF caused by injection of the bacterial cell wall component LPS by 50%. Buprenorphine has also been shown to activate mast cells, decrease liver weight, induce apoptosis, decrease corticosterone levels, and increase the incidence of pneumonia in experimental rodents. Buprenorphine, may be somewhat less immunosuppressive than morphine, as it has been used to study lymphocyte function.

### References:

1. Fox JL, Opioids appear to suppress immune system responses. ASM News 1999;65:8-9
2. Gungor M, Genc E, Sagduyu H, et. al. Effect of chronic administration of morphine on primary immune response
3. Hendrickson M, Shelby J, Sullivan JJ, et al. Naloxone inhibits the in vivo immunosuppressive effects of morphine and thermal injury in mice. J. Burn Care Rehab. 1989;10:494-8

4. Sibinga NES, Goldstein A., Opioid peptides and opioid receptors in cells of the immune system. *Ann. Rev. Immunol* 1988;6:219-49
5. Tubaro E, Borelli G, Croce C, et. al. Effect of morphine on resistance to infection. *J. infect. Dis.* 1983;148:656-66
6. Houghtling RA, Mellon RD, Tan RJ, Bayer BM. Acute effects of morphine on blood lymphocyte proliferation and plasma IL-6. *Ann N. Y. Acad. Sci.* 2000; 917:771-777
7. Roy S, Cain KJ, Charboneau RG, Barke RA. Morphine accelerates the progression of sepsis in an experimental sepsis model. 1998; 437:21-31
8. Jobin N, Garrel DR, Bernier J. Increased burn-induced immunosuppression in lipopolysaccharide-resistant mice. *Cell Immunol* 2000; 200:65-75
9. Piersma FE, Daeman MARC, vd Bogaard AEJM, Buurman WA. Interference of pain control employing opioids in in vivo immunological experiments. 1999; 33:328-333
10. Van Loveren H, Gianotten N, Hendricksen CF, Schuurman HJ, Van der Laan JW. Assessment of immunotoxicity of buprenorphine. *Lab. Anim.* 1994; 28:355-363.

Non-steroidal analgesics block production of prostaglandins , which play a role in the immunosuppression seen in burns. The nonsteroidal analgesic indomethacin, with or without interleukin therapy has been shown to improve survival and reduced leukocyte hyperactivity in burn and sepsis models. Since the principle objective of our studies relates to sepsis induced alterations in immune function and the ability of treatment regimens to improve these functions, these analgesic drugs would clearly influence the results of our study.

References

1. Santangelo S, Shoup M, Gamelli RL, Shankar R. Prostaglandin E2 receptor antagonist (SC-19220) treatment restores the balance to bone marrow myelopoiesis after burn sepsis. *J. Trauma* 2000; 48:826-831
2. Strong, VE, Mackrell PJ, Concannon EM, Naama HA, Schaefer PA, Shafeton GW, Stapelton PP, Daly JM. Blocking Prostaglandin E2 after trauma attenuates pro-inflammatory cytokines and improves survival. *Shock* 2000, 14:374-379.
3. Horgan PG, Mannick JA, Dubravec DB, Rodrick ML. Effect of low dose recombinant interleukin 2 plus indomethacin on mortality after sepsis in a murine burn model. *Br. J. Surg.* 1990. 77:401-404
4. Latter DA, Tchervenkov JI, Nohr CW, Christou NV, The effect of indomethacin on burn induced immunosuppression. *J. Surg. Res.* 1987. 43:246-252

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency \_\_\_\_\_ CFR \_\_\_\_\_

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1. Registration Number: **33-R-0029**

2. Number 111 of animals used in this study.

3. Species (common name) Pigs of animals used in the study.

4. Explain the procedure producing pain and/or distress.

We are testing the potential of a dietary change to protect young pigs from enteric disease caused by *E. coli*. We are producing a mild diarrhea and mild fever by challenging the pigs with a pathogenic strain of *E. coli*.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see question 6 below).

Treatment with antibiotics would compromise the test of the dietary treatment, and perhaps mask any benefits the diet may produce.

We are monitoring the pigs at least 3 times per day, and are prepared to euthanize pigs if they are at the end point criteria.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency \_\_\_\_\_ CFR \_\_\_\_\_

## Column E Explanation

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1. Registration Number: **33-R-0029**

2. Number   24   of animals used in this study.

3. Species (common name)   swine   of animals used in the study.

4. Explain the procedure producing pain and/or distress.

These animals were evaluated for their responses to PRRS vaccination via (b)(4) and then challenged (b)(4) with the live PRRS virus in order to assess the efficacy of the vaccination system. As the PRRS virus causes PRRS disease, with symptoms including weight loss, loss of appetite, transient fever, among others, it is anticipated that there is some level of discomfort that is experienced by the test animals during the period of 14 days following administration of the PRRS virus.

Twelve of the pigs of the PRRSV-inoculated pigs exhibited the clinical signs. These included a transient fever, lethargy, reduced feed intake and reduced weight gain. None of the symptoms were serious (and thus did not warrant antibiotic or medical treatment), and were typical of what were observed in past PRRSV-challenge experiments conducted in (b)(6), (b)(7)c lab.

None of the 12 control pigs displayed any abnormal clinical signs.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see question 6 below).

To determine whether or not the vaccine indeed provides protection against PRRS, our control pigs (not vaccinated) as well as vaccinated pigs could not be relieved of discomfort as this will directly interfere with our assessment of the efficacy of this vaccine. Typically when one animal is treated (antibiotics, medication) then so are all of the other animals to avoid any confounding effects. Since the goal of this experiment is have PRRS virus-infected pigs develop clinical signs, any type of medical treatment could potentially eliminate their response to PRRS virus. Additionally, due to the limited number of pigs utilized in this experiment, all animals were needed for terminal sample collection at the conclusion of the 14 day challenge period.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency \_\_\_\_\_ CFR \_\_\_\_\_